

In re Application of:  
Jean-Pierra Issa  
Application No.: 09/398,522  
Filed: September 15, 1999  
Exhibit A: Page 1



PATENT  
Attorney Docket No.: JHU1590

**CLAIMS AS THEY WILL STAND UPON ENTRY OF THE AMENDMENTS**

10. (Amended) A method for detecting a cellular proliferative disorder associated with APOB, CACNA1G, CDX2, EGFR, FBN1, GPR37, HSPA6, IQGAP2, KL, PAR2, PITX2, PTCH, SDC1 or SDC4 in a subject comprising:
  - a) contacting a nucleic acid-containing specimen from the subject with an agent that provides a determination of the methylation state of at least one gene or associated regulatory region of the gene;  
wherein the gene is selected from the group consisting of APOB, CACNA1G, CDX2, EGFR, FBN1, GPR37, HSPA6, IQGAP2, KL, PAR2, PITX2, PTCH, SDC1, SDC4 and combinations thereof and
  - b) identifying aberrant methylation of regions of the gene or regulatory region,  
wherein aberrant methylation is identified as being different when compared to the same regions of the gene or associated regulatory region in a subject not having said cellular proliferative disorder, thereby detecting a cellular proliferative disorder in the subject.
11. The method of claim 10, wherein the regions of said gene are contained within CpG rich regions.
13. The method of claim 10, wherein aberrant methylation comprises hypermethylation when compared to the same regions of the gene or associated regulatory regions in a subject not having the cellular proliferative disorder.

In re Application of:  
Jean-Pierre Issa  
Application No.: 09/398,522  
Filed: September 15, 1999  
Exhibit A: Page 2

PATENT  
Attorney Docket No.: JHU1590

14. The method of claim 13, wherein the regions comprise regulatory regions of CACNA1G.
15. The method of claim 14, wherein the regions comprise regions 1-8 of CACNA1G.
16. The method of claim 15, wherein the regions comprise regions 1-2 of CACNA1G.
17. The method of claim 15, wherein the regions comprise regions 5-7 of CACNA1G.
18. The method of claim 15, wherein the regions comprise regions 4 and 8 of CACNA1G.
19. The method of claim 10, wherein the agent is a pair of primers that hybridize with a target sequence in the gene or associated regulatory region of the gene.
20. The method of claim 19, wherein the primers hybridize with a target polynucleotide sequence having the sequence selected from the group consisting of SEQ ID NO:55-103 and SEQ ID NO:104.
21. (Amended) The method of claim 20, wherein the primer pair is selected from the group consisting of SEQ ID NO:1 and 2, SEQ ID NO:3 and 4, SEQ ID NO:5 and 6, SEQ ID NO:7 and 8, SEQ ID NO:9 and 10, SEQ ID NO:11 and 12, SEQ ID NO:13 and 14, SEQ ID NO:15 and 16, SEQ ID NO:17 and 18, SEQ ID NO:19 and 20, SEQ ID NO:21 and 22, SEQ ID NO:23 and 24, SEQ ID NO:25 and 26, SEQ ID NO:27 and 28, SEQ ID NO:29 and 30, SEQ ID NO:31 and 32, SEQ ID NO:33 and 34, SEQ ID NO:35 and 36, SEQ ID NO:37 and 38, SEQ ID NO:39 and 40, SEQ ID NO:41 and 42, SEQ ID NO:43 and 44, SEQ ID NO:45 and 46, SEQ ID NO:47 and 48, and SEQ ID NO:49 and 50.

In re Application of:  
Jean-Pierre Issa  
Application No.: 09/398,522  
Filed: September 15, 1999  
Exhibit A: Page 3

PATENT  
Attorney Docket No.: JHU1590

22. The method of claim 10, wherein the nucleic acid-containing specimen comprises a tissue selected from the group consisting of brain, colon, urogenital, lung, renal, prostate, pancreas, liver, esophagus, stomach, hematopoietic, breast, thymus, testis, ovarian, and uterine.
23. The method of claim 10, wherein the nucleic acid-containing specimen is selected from the group consisting of serum, urine, saliva, blood, cerebrospinal fluid, pleural fluid, ascites fluid, sputum, stool, and biopsy sample.
24. The method of claim 10, wherein said cellular proliferative disorder is selected from the group consisting of low grade astrocytoma, anaplastic astrocytoma, glioblastoma, medulloblastoma, gastric cancer, colorectal cancer, colorectal adenoma, acute myelogenous leukemia, lung cancer, renal cancer, leukemia, breast cancer, prostate cancer, endometrial cancer and neuroblastoma.